reached maturity and begun to degenerate. Between the fourth and sixth weeks the mesonephros, mesonephric duct, ureteric bud, and metanephros are undergoing active developments. The future of the kidney depends upon: (1) the successful caudal migration of the mesonephric duct; (2) the sprouting of the ureteric bud; (3) the formation of the metanephros; and (4) a combination of these three processes. The "critical period" of renal formation is between the fourth and sixth weeks of intrauterine life, and it is during this period that one would expect noxious environmental influences to be most effective.

Discussion

It is suggested that Case 1 is an example of congenital abnormality caused by disturbed environment. Six weeks after her last menstrual period, in a regular cycle of 6/27, the mother swallowed 2.3 g. (35 gr.) of a quinine salt within 24 hours, and later 85 ml. (3 fl. oz.) of an ergot mixture and two tablets of an unknown substance. The probable age of the embryo at this time—4 to 6 weeks—covered the important developmental periods of the mesonephric duet, cloaca and ureteric bud.

Quinine salts are known to be protoplasmic poisons with a specific nephrotoxic action. They are readily absorbed into the blood stream, and Dilling and Gemmell (1929) showed that quinine crosses the placental barrier at term. Huggett and Hammond (1952) state that placental permeability of different agents varies according to the stage of development. We have been unable to trace experimental proof that quinine reaches the human ovum from the maternal blood in the first few weeks of pregnancy. However, we submit that it is not unreasonable to regard quinine as the agent responsible for the agenesis of the kidneys in Case 1. Our assumption is that the drug acted direct on the rapidly differentiating renal tissue.

The deformity of the left pinna is interesting. Potter noted certain facial characteristics, which included large low-lying ears with cartilaginous dysplasia. In a six-weeks embryo the external ear is beginning development around the first branchial cleft. Therefore it may be supposed that disordered differentiation of the tissues at this time was the result of an insult, the timing of which coincided with the quinine administration.

One weakness in our hypothesis is the fact that quinine and other drugs are often taken as abortifacient measures during the early weeks of pregnancy and yet bilateral anephrogenesis is rare. There are three points to make in reply. First, the drug must be taken at the correct time in the development of the renal tract; the margin of error in time allowance is probably very small. Secondly, it is necessary to assess the incidence of anephrogenesis in the embryos and foetuses of abortions. Thirdly, the dosage and concentration of the drug must be sufficiently great.

Summary

Four cases of congenital absence of both kidneys are reported. One of these cases is described in detail.

The aetiology of the condition is discussed. The fourth to sixth weeks of embryonic life are the "critical period" during which development of the kidneys is taking place, and is the time when noxious environmental factors could exert their most damaging effects.

Quinine, taken by the mother of one case in a large dose six weeks after her last menstrual period, is suggested as a possible cause of the renal agenesis.

We wish to thank Dr. M. Dynski-Klein, Mr. D. M. Stern, and Miss I. M. Titcomb for allowing us to report these cases under their care and for access to their records; Dr. A. C. Counsell for his careful pathological examinations; and Miss S. Robinson for the drawing.

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USE OF UNSATURATED FATTY ACIDS IN THE ECZEMAS OF CHILDHOOD

BY

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Burr and Burr (1929, 1930) and Burr *et al.* (1932) showed that the total exclusion of fats from the diet of young rats produced a deficiency disease with caudal necrosis, red and somewhat swollen feet, and scaliness in the hair of the back. At the same time the growth of the animals was arrested and there was much loss of weight. This condition was not improved by adding non-saponifiable fats to the diet, but was cured by the unsaturated fatty acids (U.F.A.s), particularly linoleic and linolenic acids.

This work stimulated Hansen (1933), who first made the suggestion that U.F.A.s might be useful in treating infantile eczema. He demonstrated that there was a diminution of these acids in the serum of eczematous children, and he claimed that the addition of U.F.A.s to their diet caused a clinical improvement which was associated with a rise in the iodine number, an index of the non-saturated fatty acids in the serum. Shortly afterwards Cornbleet (1935) reported good results in a series of 85 cases of eczema which had been treated with fresh lard by mouth, but there seems to be no reference to any control in his investigation. Taub and Zakon (1935) found no benefit in eight cases of atopic eczema (Besnier's prurigo, disseminated neurodermatitis) which they treated with linseed oil by mouth, and also pointed out that the use of linseed or cotton-seed oil might be dangerous, as the patient could be sensitive to these sources of U.F.A.s. Ginsberg and Bernstein (1937) found satisfactory improvement in three adults in a group of 11 with atopic dermatitis and in four out of six children. They also pointed out, however, that two children receiving the same local treatment and no added U.F.A.s improved in the same time. Finnerud, Kesler, and Weise (1941), using fresh lard in older children and adults, had a satisfactory response in about half their cases. Hansen, Knott, *et al.* (1947) reported on the study of 225 cases of eczema, of whom 123 were under the age of 2 years, 67 were from 2 to 15, and 35 were 16 and over. During these trials they used many forms of local treatment, including boric acid, zinc paste, sulphur, resorcinol, and occasionally coal-tar. Their results were poor in only 37 of the 148 cases treated with supplementary fatty acids, while 18 of the 48 controls were unsatisfactory in the same

period. They also demonstrated that the iodine number is reduced in many cases of eczema and returns to normal on satisfactory treatment.

More recently European workers have stepped into this field with investigations and reports on lines similar to those of the earlier American articles. As early as 1942 Justin-Besançon and Laroche criticized those who saw fit to call linoleic acid "vitamin F," and also pointed out that the administration of U.F.A.s gave very divergent results and that "the conclusion that certain authors wish to draw seems insecurely based." Azerad and Grupper (1949a) summed up their experience and claimed that lard by mouth was giving extremely encouraging results, but later (1949b) they reported better results with purified linoleic acid. In 58 breast-fed infants, 18 children, and 24 adults whom they treated they obtained 52 excellent or good results, and only 17 were mediocre or negligible. It must be pointed out that the linoleic acid was only a supplementary form of treatment, and as local treatment they used "nothing except a paste or ointment of 10% tar," which they deliberately chose in view of the excellent action of tar on vesicular and weeping eczema. Touraine (1949) quotes Pätiälä (1948), who found an improvement in infantile eczema treated with vitamin B_6; and Charpy (1948) combined this with the U.F.A.s and claimed there was a synergistic effect, but Hansen was unable to confirm this. Touraine also quotes Vachon (1948) as having tried the application of 3% linoleic acid in an ointment base, which was found to irritate, and he used a 1% ointment in resistant cases but said it should be employed with care. Alechinsky (1950) claimed six complete cures in 11 cases, while Dubois (1950), summing up the Continental view, pointed out that local treatment, preferably tar, was indispensable and claimed that irritation ceased in four to seven days and exudation dried in two to four days. More recently Finzi (1951) and Carletti and Scalamogna (1952) claimed good results, but in an apparently uncontrolled series of cases.

The unsatisfactory state of these claims and the associated recent publicity in this country of the use of unsaturated fatty acids, particularly linoleic and linolenic acids in liquid, ointment, and capsule form, suggested that an investigation of their effectiveness should be undertaken.

The following investigations were therefore carried out at a hospital mainly for the long-term treatment of children with severe and chronic dermatoses.

Local Application and Oral Administration of U.F.A.s

For the first investigation 27 cases of infantile and atopic eczema were used. The ages ranged from 18 months to 15 years, and so far as was possible the cases were paired in age and type of skin lesion. The babies with infantile eczema had usually been in hospital only a short time, while most of the older children had spent a considerable period in hospital. As a result of this long-term treatment any improvement which might have been attributed to the child's change of environment on admission to hospital was, in the main, avoided.

Each child was seen at the start of the trial and assessed, and after that, without the investigator's knowledge of which children were being treated, 15 children were given a daily application of an ointment with the following formula:

Linoleic acid	1.7%
Linolenic acid	0.8%
Hydrous ointment .. .. to	100%

and orally a capsule a day:

Linoleic acid	0.27 g.
Linolenic acid	0.13 g.
Arachis oil .. .. .. to	0.5 g.

The other 12 children continued the routine treatment of the hospital, usually zinc ointment with boric acid and various strengths of tar. An independent dermatologist (Dr. G. B. Dowling) also saw the patients regularly, and if the child's condition deteriorated enough to warrant a change of treatment the case was automatically graded as −2. Each child was seen and assessed weekly, and at the end of seven weeks the progress was marked in the following way:

Improvement amounting almost to cure	+2
Overall improvement	+1
Approximately the same as at the start	0
Overall deterioration	−1
Failure, needing change of treatment	−2

It was not until all these cases were marked that the investigator knew which patients were being treated with the U.F.A.s. In that way any bias for or against the treatment was avoided.

The results (Table I) showed no evidence that the treatment with local and oral unsaturated fatty acids was a satisfactory substitute for the normal routine. The possibility

TABLE I

	+2	+1	0	−1	−2	Total
Cases on local and oral U.F.A.s	1	0	1	8	5	15
Cases on usual treatment ..	3	5	2	1	1	12

that the ointment itself might irritate was considered, but the fact that one child steadily improved while on the treatment disproved this. Later, at the end of the series, patch tests with the ointment were made in cases that had failed, but no evidence of sensitivity to the ointment was found. It was thought that this group of cases showed striking evidence against the further continuation of the trial, but in order to assess whether oral U.F.A.s in addition to the routine hospital treatment was of benefit a further investigation was made.

Oral U.F.A.s as an Adjuvant to Therapy

This group consisted of 36 cases of infantile eczema and atopic eczema, 20 of whom took a capsule of linoleic and linolenic acid daily for approximately four months. The actual time that patients were treated varied from nine to seventeen weeks. Several of the children were discharged from hospital in this time and they were automatically marked +2. Again any child whose treatment was altered because of manifest deterioration was graded −2.

TABLE II

	+2	+1	0	−1	−2	Total
Routine treatment plus oral U.F.A.	7	8	3	2	0	20
Routine treatment	8	3	3	1	1	16

Taking into consideration the slightly smaller group of controls, it is not considered that this investigation produced any evidence that oral U.F.A.s have value as an adjunct to local treatment of infantile or atopic eczema.

Discussion

The diminution of the iodine number showing the reduction of U.F.A.s in the serum of children with eczema caused Hansen to start this long and contradictory series of investigations. The conception that a reduction in the U.F.A.s of the serum is aetiologically connected with infantile eczema was doubted by Faber and Roberts (1933), who found that in eczema the cholesterol was slightly higher, the total fatty acid and the total lipid content considerably higher, and an iodine number only moderately lower than in normal controls. They did not find a degree of unsaturation as high as Hansen did, and expressed a belief that the findings were secondary rather than causative. This suggestion would seem to receive support from Hansen's own work, which shows there is a rise in the iodine number in children satisfactorily treated for eczema with nothing but local applications of tar (Hansen, 1933; Hansen, Knott, *et al.*, 1947).

The emphasis placed by nearly all authors who claim benefit from the use of these fatty acids on the fact that

local treatment is a prime necessity, and the apparent lack of any great interest in a controlled series, suggest that the benefits claimed may be due to the usual treatment, with perhaps a dash of enthusiasm.

The investigations reported here, in which all personal bias and normally varying factors were removed so far as was possible, have failed to substantiate the claims that the so-called "vitamin F" has any value in the treatment of atopic and infantile eczema. The findings of Vachon seem to be borne out, in that the ointment almost invariably irritated the eczematous skin.

Summary

A brief summary of the literature on the use of unsaturated fatty acids in the treatment of infantile and atopic eczema is followed by the details of a recent investigation.

The combined use of linoleic and linolenic acid ointment and capsules and the use of the capsules as an adjuvant to routine treatment were in no way preferable to the established methods of treatment.

My thanks are due to Dr. G. B. Dowling for allowing me to see and investigate his cases, and to the matron and nursing staff of the Goldie Leigh Hospital for their willing co-operation.

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Medical Memoranda

Total Gastrectomy for Haematemesis

The object of this report is to point out the necessity for total gastrectomy in certain rare cases of haematemesis and to stress the value of oesophagoscopy in diagnosing the source of the haemorrhage.

Obvious bleeding occurs in some 20% of all peptic ulcers, and these form about 85% of all cases of haematemesis and melaena. The total mortality rate in the peptic ulcer group is roughly 8%, but in patients under 45 it is 2%. Death more often takes place from irreversible changes following prolonged anoxia than from acute anaemia, as necropsy nearly always shows the vessel occluded by clot. Hence the sheet anchor of treatment is blood transfusion, not only to prevent anoxia but also to enable the patient to withstand further haemorrhage by keeping the haemoglobin level about 80%. If this rule is followed the so-called critical periods on the third day or at any other time cease to exist, and surgery is indicated when replacement does not control the loss or if the loss continues or recurs for several days.

HAEMORRHAGE FROM FUNDUS OF STOMACH AND LOWER OESOPHAGUS

The importance of haemorrhage from the fundus of the stomach was first impressed upon me by a patient, known to be suffering from a chronic gastric ulcer for some years, who was admitted with severe haematemesis which did not respond satisfactorily to transfusion. A partial gastrectomy was successful, but the specimen showed that the bleeding was not from the known chronic ulcer but from a small acute ulcer high up the lesser curvature which had been included in the resected area by luck, not judgment. This acute ulcer was not palpable to the gloved finger, and I doubt if it would have been noticed on gastrotomy, which in other cases has proved to be of no value.

Further, the importance to the differential diagnosis of the site of the haemorrhage was brought home by another man, known to have a chronic gastric ulcer, who was admitted with severe haematemesis not controlled by transfusion. At partial gastrectomy cirrhosis of the liver was noted. He died five days later from continued bleeding from oesophageal varices. No evidence of haemorrhage from the ulcer was found. This error might have been prevented by an oesophagoscopic examination, in which it is simple to distinguish a normal oesophagus, a normal oesophagus with regurgitated blood in it, bleeding oesophageal varices, or a stomach distended by gastric haemorrhage. In fact, since then it has saved me from making the same mistake again.

Those who are not trained in the use of the common instruments for the visualization of their patients' orifices will find no difficulty in passing an appropriate-sized oesophagoscope if they will first pass a stomach tube, aspirate, and then pass the endoscope alongside it before its removal.

Treatment.—This must be governed by the general principles already mentioned. When surgery is indicated for gastric haemorrhage from acute ulceration it is no use temporizing by doing a gastro-enterostomy (as in my house-surgeon days) or a partial gastrectomy or ligation of gastric vessels (as is often done now). I know of deaths from continuing haemorrhage after these procedures have been carried out by competent surgeons and also of recovery when nothing has been done. Acute fundic ulceration is probably as common as is acute ulceration in any other part of the stomach, and unless at laparotomy the surgeon can determine the site of bleeding he is faced with only two logical procedures: nothing or total gastrectomy. The following case histories illustrate the problem.

CASE 1

An engineer aged 58 collapsed at work on March 16, 1952, and was admitted to Lodge Moor Hospital the next day as a case of "influenzal pneumonia." No cause for his collapse was found on admission, but 48 hours later he had a severe haematemesis. Blood transfusion was at once started, and he was transferred later in the day (March 19) to the City General Hospital. His pulse was 130 and blood pressure 105/60, and he was pale, cold, and clammy. Further transfusion was given, with improvement.

On March 21 he had further haematemesis and melaena in spite of a total of 8 pints (4.5 litres) of blood, so I was asked to see him with a view to surgery. His pulse was 84, blood pressure 85/55, Hb 8.8 g. (60%). He gave a history of several weeks of epigastric discomfort after food lasting an hour or so, and then complete freedom for several days before the next recurrence. I felt that the diagnosis of a chronic ulcer or carcinoma was very unlikely and suggested further conservative treatment.

However, on March 26 his condition deteriorated in spite of a total of 21 pints (11.9 litres) of blood, and laparotomy was advised.

First Operation.—On March 26, under intratracheal gas and oxygen, thiopentone, and D-tubocurarine chloride, a left upper paramedian incision was made. External exploration of the stomach and duodenum showed no lesion or evidence of scarring from an old lesion. The intestines were full of blood. The anterior stomach wall was incised from the lesser to the greater curvature roughly at its mid-point and the contents were aspirated. No fresh blood was present, but some adherent clot at the fundus was found. Nothing abnormal was seen or palpated though ungloved hands were used. The lower oesophagus also felt normal. The problem was total gastrectomy or nothing, and I chose the latter